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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/029,913	12/31/2001	Ulf Landegren	LAND DIV	5983
466	7590	05/26/2006	EXAMINER	
YOUNG & THOMPSON 745 SOUTH 23RD STREET 2ND FLOOR ARLINGTON, VA 22202			FORMAN, BETTY J	
			ART UNIT	PAPER NUMBER
			1634	

DATE MAILED: 05/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/029,913

Applicant(s)

LANDEGREN, ULF

Examiner

BJ Forman

Art Unit

1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 March 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 33-35 and 38-46 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 33-35 and 38-46 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____

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FINAL ACTION

Status of the Claims

1. This action is in response to papers filed 9 March 2006 in which claim 33 was amended, claims 36-37 were canceled and claims 43-46 were added. All of the amendments have been thoroughly reviewed and entered.

The previous rejections in the Office Action dated 9 September 2005 are withdrawn in view of the amendments. Applicant's arguments have been thoroughly reviewed but are deemed moot in view of the amendments, withdrawn rejections and new grounds for rejection. New grounds for rejection, necessitated by amendment, are discussed.

The examiner for this application has changed. Please address future correspondence to Examiner BJ Forman, Art Unit: 1634.

Claims 33-35 and 38-46 are under prosecution.

Claim Rejections - 35 USC § 112

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 43-46 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 43-46 are indefinite for recitations within parenthesis e.g. "(padlock)" and "(or de-connected)". Recitations within parenthesis are deemed indefinite because it is unclear whether the recitations further define limitations of the claims.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 33 and 38-42 are rejected under 35 U.S.C. 102(b) as being anticipated by Kwiatkowski (WO 95/226323, published 24 August 1995).

Regarding Claim 33, Kwiatkowski discloses methods of target detection comprising providing an immobilized probe (e.g. page 11, lines 16-27 and Claim 12) wherein the probe has a 3' and 5' end wherein one of the ends is provided with a solid phase anchor (e.g. via hybridization, Fig. 1 and/or page 11, line 20) and the other end comprises a detectable function (e.g. detectable via intermediate probe, page 7, lines 10-18) and cleaveable or dissociable site (e.g. subject to denaturation and/or exonuclease digestion, page 7, line 37-page 8, line 2). The method comprises contacting the probe with a target, covalently connecting probe ends to circularize, cleaving or dissociating wherein if the probe is circularized, the detectable function is covalently connect to the support (i.e. intermediate probe is ligated to the probe ends forming "covalent closure" of the probe which is immobilized, Fig. 1 and page 7) and detecting the presence of the detectable function (Claims 1-12).

Regarding Claim 38, Kwiatkowski et al discloses the method wherein the probe ends hybridize to the target leaving an interspace where a third probe hybridizes and covalently connects the probe ends (page 7, Claim 2).

Regarding Claim 39, Kwiatkowski et al discloses the method wherein the probe ends hybridize to the target leaving an interspace where an extension reaction fills the space to covalently connects the probe ends (Claim 3).

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Regarding Claim 40, Kwiatkowski et al discloses the method wherein the covalent connection is via enzymatic, ribozyme-mediated or chemical ligation (Claim 4).

Regarding Claim 41, Kwiatkowski et al disclose the method wherein the target is DNA or RNA (page 10, lines 12-13).

Regarding Claim 42, Kwiatkowski et al disclose the method wherein the probes are immobilized via biotin to a streptavidin-coated solid phase (page 13, lines 16- page 14, line 30).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

7. Claims 34-35 and 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kwiatkowski (WO 95/226323, published 24 August 1995) in view of Urdea et al (U.S. Patent No. 5,124,246, issued 23 June 1992).

Regarding Claims 34-35 and 42, Kwiatkowski discloses methods of target detection comprising providing an immobilized probe (e.g. page 11, lines 16-27 and Claim 12) wherein the probe has a 3' and 5' end wherein one of the ends is provided with a solid phase anchor (e.g. via hybridization, Fig. 1 and/or page 11, line 20) and the other end comprises a detectable function (e.g. detectable via intermediate probe, page 7, lines 10-18) and cleavable or dissociable site (e.g. subject to denaturation and/or exonuclease digestion, page 7, line 37-page 8, line 2). The method comprises contacting the probe with a target, covalently connecting probe ends to circularize, cleaving or dissociating wherein if the probe is circularized, the

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detectable function is covalently connect to the support (i.e. intermediate probe is ligated to the probe ends forming “covalent closure” of the probe which is immobilized, Fig. 1 and page 7) and detecting the presence of the detectable function (Claims 1-12). Kwiatkowski et al do not teach branched probes.

However, immobilized and branched probes were well known in the art at the time the claimed invention was made as taught by Urdea et al.

Urdea et al. teaches the above method wherein one or both of the probe ends have at least two branches, and a detectable function is provided on each of the branches on one end part of said probe, the detectable functions being different and distinguishable from each other and a circularizable probe comprising two free cleavable or detectable nucleic acid end parts which are linear, branched or bifurcated and are capable of hybridizing to two at least substantially neighboring regions of a target sequence (abstract, examples 1, 2 and 3). Specifically, in Column 17 lines 45-55, Urdea teaches that various techniques may be employed for detecting the presence of the label.

Urdea et al further teach in Column 16 lines 29-31 oligonucleotide probes attached to solid phase via “biotin/avidin”.

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the branched or bifurcated probes of Urdea et al. and the ligand receptor binding pair of “biotin/avidin” in the method of Nilsson et al. since Urdea et al state, “suitable cleavable linker molecules may be incorporated into the multimers at predetermined sites for the purpose of analyzing the structure of the multimer or as a means for releasing predetermined segments (such as the portion of the multimer that binds to the oligonucleotide) (Column 12, lines 49-55)99. Moreover, Urdea et al. states “The multimers may be used in essentially any of the known nucleic acid hybridization formats, such as those in which the analyte is bound directly to a solid phase or a sandwich hybridization in which the analyte is bound to an oligonucleotide that is in turn bound to a solid phase (Column 13, lines

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56-61)". An ordinary practitioner would have been motivated to combine and substitute the branched or bifurcated probes of Urdea et al. into the method of Nilsson et al. in order to achieve the express advantages, as noted by Urdea et al., of improving the sensitivity of nucleic acid based assay by applying multimers, which may be used in essentially any of the known nucleic acid hybridization formats, such as those in which the analyte is bound directly to a solid phase or sandwich hybridization in which the analyte is bound to an oligonucleotide that is in turn bound to a solid phase.

Double Patenting

8. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

9. Claims 33-35 and 38-46 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-16 and 20 of U.S. Patent No. 6,558,928 in view of Urdea et al (U.S. Patent No. 5,124,246, issued 23 June 1992).

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Although the conflicting claims are not identical, they are not patentably distinct from each other because both sets of claims are drawn to methods of target detection comprising steps of forming circular/padlock probes. The claims sets merely differ in that instant claims define the probes as having an anchor for immobilization of the probe and claims 34-35 further define the probes as having branches. However, immobilized and branched probes were well known in the art at the time the claimed invention was made as taught by Urdea et al.

Urdea et al. teaches the above method wherein one or both of the probe ends have at least two branches, and a detectable function is provided on each of the branches on one end part of said probe, the detectable functions being different and distinguishable from each other and a circularizable probe comprising two free cleavable or detectable nucleic acid end parts which are linear, branched or bifurcated and are capable of hybridizing to two at least substantially neighboring regions of a target sequence (abstract, examples 1, 2 and 3). Specifically, in Column 17 lines 45-55, Urdea teaches that various techniques may be employed for detecting the presence of the label.

Urdea et al further teach in Column 16 lines 29-31 oligonucleotide probes attached to solid phase via "biotin/avidin".

Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute the branched or bifurcated probes of Urdea et al. and the ligand receptor binding pair of "biotin/avidin" in the method of Nilsson et al. since Urdea et al state, "suitable cleavable linker molecules may be incorporated into the multimers at predetermined sites for the purpose of analyzing the structure of the multimer or as a means for releasing predetermined segments (such as the portion of the multimer that binds to the oligonucleotide) (Column 12, lines 49-55)99. Moreover, Urdea et al. states "The multimers may be used in essentially any of the known nucleic acid hybridization formats, such as those in which the analyte is bound directly to a solid phase or a sandwich hybridization in which the analyte is bound to an oligonucleotide that is in turn bound to a solid phase (Column 13, lines

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10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to BJ Forman whose telephone number is (571) 272-0741. The examiner can normally be reached on 6:00 TO 3:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on (571) 272-0735. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.


BJ Forman, Ph.D.
Primary Examiner
Art Unit: 1634
May 22, 2006